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FEB 0 5 2002

TECH CENTER 1600/2900

<110> McKeon, F. Kayako, K. Ryeom, S.

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<140> 09/575,580 <141> 2000-05-22

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Lys Ser Phe Lys Arg Val Arg Ile Asn Phe Ser Asn Pro Leu Ser Ala 50 55 60

Ala Asp Ala Arg Leu Arg Leu His Lys Thr Glu Phe Leu Gly Lys Glu 65 70 75 80

Met Lys Leu Tyr Phe Ala Gln Thr Leu His Ile Gly Ser Ser His Leu 85 90 95

Ala Pro Pro Asn Pro Asp Lys Gln Phe Leu Ile Ser Pro Pro Ala Ser 100 105 110

Pro Pro Val Gly Trp Lys Gln Val Glu Asp Ala Thr Pro Val Ile Asn 115 120 125

Tyr Asp Leu Leu Tyr Ala Ile Ser Lys Leu Gly Pro Gly Glu Lys Tyr 130 135 140

Glu Leu His Ala Ala Thr Asp Pro Thr Pro Ser Val Val His Val
145 150 155 160

Cys Glu Ser Asp Gln Glu Asn Glu Glu Glu Glu Glu Glu Met Glu Arg
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Thr Pro Ile His Leu Ser 195

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35 40 45

Leu Thr Asp Phe Ser Asp Leu Pro Asn Ser Leu Phe Ala Cys Asn Val 50 55 60

BI Jewr His Gln Ser Val Phe Glu Glu Glu Glu Ser Lys Glu Lys Phe Glu Gly 65 70 75 80

Leu Phe Arg Thr Tyr Asp Glu Cys Val Thr Phe Gln Leu Phe Lys Ser 85 90 95

Phe Arg Arg Val Arg Ile Asn Phe Ser His Pro Lys Ser Ala Ala Arg 100 105 110

Ala Arg Ile Glu Leu His Glu Thr Gln Phe Arg Gly Lys Lys Leu Pro 115 120 125

Leu Tyr Phe Ala Gln Val Gln Thr Pro Glu Thr Asp Gly Asp Lys Leu 130 135 140

His Leu Ala Pro Pro Gln Pro Ala Lys Gln Phe Leu Ile Ser Pro Pro 145 150 155 160

Ser Ser Pro Ser Val Gly Trp Lys Pro Ile Ser Asp Ala Thr Pro Val 165 170 175

Leu Asn Tyr Asp Leu Leu Tyr Ala Val Ala Lys Leu Gly Pro Gly Glu 180 185 190

Lys Tyr Glu Leu His Ala Gly Thr Glu Ser Thr Pro Ser Val Val
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His Val Cys Asp Ser Asp Met Glu Arg Glu Glu Asp Pro Lys Thr Ser 210 215 220

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Thr Tyr Asp Asp Cys Val Thr Phe Gln Leu Phe Lys Ser Phe Arg Arg
35 40 45

Val Arg Ile Asn Phe Ser Asn Pro Lys Ser Ala Ala Arg Ala Arg Ile
50 55 60

Glu Leu His Glu Thr Gln Phe Arg Gly Lys Lys Leu Lys Leu Tyr Phe 65 70 75 80 Ala Gln Val Gln Thr Pro Glu Thr Asp Gly Asp Lys Leu His Leu Ala 85 90 95

Pro Pro Gln Pro Ala Lys Gln Phe Leu Ile Ser Pro Pro Ser Ser Pro 100 105 110

Pro Val Gly Trp Gln Pro Ile Asn Asp Ala Thr Pro Val Leu Asn Tyr 115 120 125

Asp Leu Leu Tyr Ala Val Ala Lys Leu Gly Pro Gly Glu Lys Tyr Glu 130 135 140

Leu His Ala Gly Thr Glu Ser Thr Pro Ser Val Val Val His Val Cys
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Ser Asn Pro Phe Ser Ala Ala Asp Ala Arg Leu Gln Leu His Lys Thr 35 40 45

Glu Phe Leu Gly Lys Glu Met Lys Leu Tyr Phe Ala Gln Thr Leu His 50 55 60

Ile Gly Ser Ser His Leu Ala Pro Pro Asn Pro Asp Lys Gln Phe Leu 65 70 75 80

Ile Ser Pro Pro Ala Ser Pro Pro Val Gly Trp Lys Gln Val Glu Asp
85 90 95

Ala Thr Pro Val Ile Asn Tyr Asp Leu Leu Tyr Ala Ile Ser Lys Leu 100 105 110

Gly Pro Gly Glu Lys Tyr Glu Leu His Ala Ala Thr Asp Thr Thr Pro 115 120 125

Ser Val Val His Val Cys Glu Ser Asp Gln Glu Lys Glu Glu Glu

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Arg Arg Pro Glu Tyr Thr Pro Ile His Leu 165 170

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Glu Ser Leu Phe Arg Thr Tyr Asp Lys Asp Ile Thr Phe Gln Tyr Phe 35 40 45

Lys Ser Phe Lys Arg Val Arg Ile Asn Phe Ser Asn Pro Leu Ser Ala 50 55 60

Ala Asp Ala Arg Leu Gln Leu His Lys Thr Glu Phe Leu Gly Lys Glu 65 70 75 80

Met Lys Leu Tyr Phe Ala Gln Thr Leu His Ile Gly Ser Ser His Leu 85 90 95

Ala Pro Pro Asn Pro Asp Lys Gln Phe Leu Ile Ser Pro Pro Ala Ser 100 105 110

Pro Pro Val Gly Trp Lys Gln Val Glu Asp Ala Thr Pro Val Ile Asn 115 120 125

Tyr Asp Leu Leu Tyr Ala Ile Ser Lys Leu Gly Pro Gly Glu Lys Tyr 130 135 140

Glu Leu His Ala Ala Thr Asp Thr Thr Pro Ser Val Val Val His Val
145 150 155 160

Cys Glu Ser Asp Gln Glu Asn Glu Glu Glu Glu Met Glu Arg Met
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Pro Ile His Leu Ser 195

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Ile Val Thr Gln Val Pro Glu Asp Val Phe Asp Asn Lys Gln Asp Lys
35 40 45

Ala Asn Phe Ser Ser Leu Phe Thr Gln Ile Glu Lys Asp Ile His Phe 50 55 60

Asp Phe Leu Arg Ser Phe Arg Arg Val Arg Val Ile Phe Ser Ser Pro 65 70 75 80

Glu Asn Ala Thr Ala Ala Lys Leu Ile Val Gln Gly Phe Ser Phe Lys 85 90 95

Gly His Glu Leu Lys Ala Phe Phe Ala Gln Arg Ile Tyr Met Ser Ala 100 105 110

Asn Ser Gln Met Leu Ser Pro Pro Pro Leu Glu Lys Gln Phe Leu Ile 115 120 125

Ser Pro Pro Cys Ser Pro Pro Val Gly Trp Glu Gln Thr Lys Asp Met 130 135 140

Pro Pro Val Val Cys Asn Phe Asp Leu Met Ala Arg Leu Ala Ser Phe 145 150 155 160

Ala Ile Asp Glu Lys Tyr Glu Val His Asn Gly Asp Glu Leu Thr Pro 165 170 175

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Lys Asn Ile Leu Arg Lys Phe Gln Ile Asn Glu Asn Glu Pro Leu Gln

35 40 45

Leu Ile Ile Leu Lys Arg Phe Lys Arg Ile Leu Leu Ile Cys Pro Ser
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His Asp Ile Ser Gln His Val Met Asp Ala Ser Arg Ala Leu Glu Met 65 70 75 80

Glu Asn Phe Asn Phe Ser Tyr Ser Leu Gln Asp Gly Gln Arg Asn Leu 85 90 95

Thr Lys Gln Tyr Leu Lys Val Pro Glu Ser Glu Lys Met Phe Leu Ile 100 105 110

Ser Pro Pro Ala Ser Pro Pro Pro Glu Phe Asp Phe Ser Lys Cys Glu 115 120 125

Asp Ala Pro Gln Arg His Ile Gln Ser His Ile Gln Gln Asp Gln Gln 130 135 140

Gln Arg Leu Glu Ala Ser Gln Leu Leu Pro Asn Asn Pro Asp Lys Asn 145 150 155 160

Asn Asn Gly Thr Phe Thr Leu Leu Lys Ser Lys Val Gly Ala Ile Thr 165 170 175

Ile Asp Arg Cys Pro Thr Asn Asp Gly Asn Gly Gln Met Gln Leu Ala 180 185 190

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Thr Leu Lys Lys Ser Ser Thr Gly Ser Leu Pro Ser Gly Gln Gln Val
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His Cys Gln Tyr Val Leu Asp Asp Pro Asn His Val Glu Gly Ile Ser 65 70 75 80

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Leu Phe Ala Cys Ser Val His Glu Ala Val Phe Glu Val Gln Glu Gln 50 55 60

Lys Glu Arg Phe Glu Ala Leu Phe Thr Leu Tyr Asp Asp Gln Val Thr
65 70 75 80

Phe Gln Leu Phe Lys Ser Phe Arg Arg Val Arg Ile Asn Phe Ser Lys 85 90 95

Pro Ala Arg Ala Arg Ile Glu Leu His Glu Ser Glu Phe His Gly Arg 100 105 110

Lys Leu Lys Leu Tyr Phe Ala Gln Val Gln Val Ser Gly Glu Ala Arg 115 120 125

Asp Lys Ser Tyr Leu Leu Pro Pro Gln Pro Thr Lys Gln Phe Leu Ile 130 135 140

Ser Pro Pro Ala Ser Pro Pro Val Gly Trp Lys Gln Ser Glu Asp Ala 145 150 155 160

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Pro Gly Glu Lys Tyr Glu Leu His Ala Gly Thr Glu Ser Thr Pro Ser 180 185 190

Val Val His Val Cys Glu Ser Glu Thr Glu Glu Glu Asp Thr
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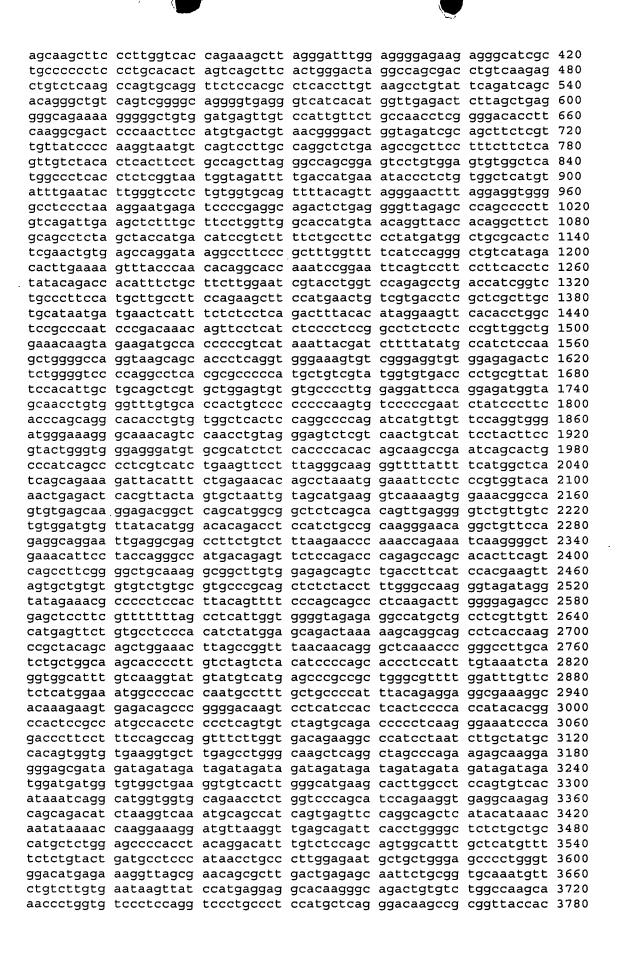
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<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: general
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<220>
<221> SITE
<222> (6)
<223> Xaa=any amino acid residue
Pro Lys Pro Lys Ile Xaa Gln Thr Arg Arg Pro Glu
                  5
                                     10
<210> 29
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<220>
<223> Description of Artificial Sequence: calcineurin
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antagonist

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<400> 29
Pro Lys Pro Lys Ile Ile Gln Thr Arg Arg Pro Glu
                  5
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<223> Description of Artificial Sequence: calcineurin
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<211> 12
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<213> Artificial Sequence
<223> Description of Artificial Sequence: EGF-derived
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Cys Met His Ile Glu Ser Leu Asp Ser Tyr Thr Cys
                  5
<210> 32
<211> 12
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<223> Description of Artificial Sequence: EGF-derived
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<400> 32
Cys Met Tyr Ile Glu Ala Leu Asp Lys Tyr Ala Cys
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<223> Description of Artificial Sequence: pH-dependent
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<220>
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<222> (1)
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      internalizing peptide to a targeting protein
      conjugate
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<221> SITE
<222> (2)..(3)
<223> Xaa=residues selected to modulate the affinity of
      the internalizing peptide for different membranes
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Gly Asn Ala Ala Ala Arg Arg
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<221> CDS
<222> (4)..(75)
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                      5
     1
                                         10
```

							gga Gly								<i>:</i> ,	75
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	0> 3 Gly		Cys	Arg 5	Gly	Asp	Met	Phe	Gly 10	Cys	Gly	Ala	Pro	Pro 15	Lys	
Lys	Lys	Arg	Lys 20	Val	Ala	Gly	Phe									
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<220> <223> Description of Artificial Sequence: synthetic construct																
<220> <221> CDS <222> (4)(225)																
		gag					aga Arg									48
							acc Thr									96
							ata Ile									144
							cga Arg 55									192
							aag Lys									225

<210> 38 <211> 74 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: synthetic construct <400> 38 Met Glu Pro Val Asp Pro Arg Leu Glu Pro Trp Lys His Pro Gly Ser Gln Pro Lys Thr Ala Cys Thr Asn Cys Tyr Cys Lys Lys Cys Cys Phe His Cys Gln Val Cys Phe Ile Thr Lys Ala Leu Gly Ile Ser Tyr Gly Arg Lys Lys Arg Arg Gln Arg Arg Pro Pro Gln Gly Ser Gln Thr 55 His Gln Val Ser Leu Ser Lys Gln Gly Phe 70 <210> 39 <211> 912 <212> DNA <213> Artificial Sequence <223> Description of Artificial Sequence: synthetic construct <220> <221> CDS <222> (4)..(912) <400> 39 cat atg acc tot ogo ogo too gtg aag tog ggt oog ogg gag gtt oog Met Thr Ser Arg Arg Ser Val Lys Ser Gly Pro Arg Glu Val Pro cgc gat gag tac gag gat ctg tac tac acc ccg tct tca ggt atg gcg 96 Arg Asp Glu Tyr Glu Asp Leu Tyr Tyr Thr Pro Ser Ser Gly Met Ala 20 25 agt coc gat agt cog cot gac acc toc cgc cgt ggc gcc cta cag aca 144 Ser Pro Asp Ser Pro Pro Asp Thr Ser Arg Arg Gly Ala Leu Gln Thr 35 ege teg ege cag agg gge gag gte egt tte gte cag tae gae gag teg 192 Arg Ser Arg Gln Arg Gly Glu Val Arg Phe Val Gln Tyr Asp Glu Ser 50 gat tat gcc ctc tac ggg ggc tcg tca tcc gaa gac gac gaa cac ccg 240 Asp Tyr Ala Leu Tyr Gly Gly Ser Ser Ser Glu Asp Asp Glu His Pro

	gtc Val			_		_		_				_	_		288
80			J		85	•				90				95	
	gly aaa														336
	cgc Arg														384
	act Thr														432
	tcg Ser 145	_	_		_		_	_			_	_		 _	480
	gcg Ala														528
_	cac His		_		_					_					576
	gtg Val	_				_		_		_	_	-	_	 	624
	gcg Ala														672
	cgt Arg 225					Glu		Leu	Asn	Glu					720
	atc Ile														768
	gag Glu														816
	act Thr														864
	cca Pro														912

290 295 300

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Asp	Glu	Tyr	Glu 20	Asp	Leu	Tyr	Tyr	Thr 25	Pro	Ser	Ser	Gly	Met 30	Ala	Ser
Pro	Asp	Ser 35	Pro	Pro	Asp	Thr	Ser 40	Arg	Arg	Gly	Ala	Leu 45	Gln	Thr	Arg
Ser	Arg 50	Gln	Arg	Gly	Glu	Val 55	Arg	Phe	Val	Gln	Tyr 60	Asp	Glu	Ser	Asp
Tyr 65	Ala	Leu	Tyr	Gly	Gly 70	Ser	Ser	Ser	Glu	Asp 75	Asp	Glu	His	Pro	Glu 80
Val	Pro	Arg	Thr	Arg 85	Arg	Pro	Val	Ser	Gly 90	Ala	Val	Leu	Ser	Gly 95	Pro
Gly	Pro	Ala	Arg 100	Ala	Pro	Pro	Pro	Pro 105	Ala	Gly	Ser	Gly	Gly 110	Ala	Gly
Arg	Thr	Pro 115	Thr	Thr	Ala	Pro	Arg 120	Ala	Pro	Arg	Thr	Gln 125	Arg	Val	Ala
Thr	Lys 130	Ala	Pro	Ala	Ala	Pro 135	Ala	Ala	Glu	Thr	Thr 140	Arg	Gly	Arg	Lys
Ser 145	Ala	Gln	Pro	Glu	Ser 150	Ala	Ala	Leu	Pro	Asp 155	Ala	Pro	Ala	Ser	Thr 160
Ala	Pro	Thr	Arg	Ser 165	Lys	Thr	Pro	Ala	Gln 170	Gly	Leu	Ala	Arg	Lys 175	Leu
His	Phe	Ser	Thr 180	Ala	Pro	Pro	Asn	Pro 185	Asp	Ala	Pro	Trp	Thr 190	Pro	Arg
Val	Ala	Gly 195	Phe	Asn	Lys	Arg	Val 200	Phe	Cys	Ala	Ala	Val 205	Gly	Arg	Leu
Ala	Ala 210	Met	His	Ala	Arg	Met 215	Ala	Ala	Val	Gln	Leu 220	Trp	Asp	Met	Ser
Arg 225	Pro	Arg	Thr	Asp	Glu 230	Asp	Leu	Asn	Glu	Leu 235	Leu	Gly	Ile	Thr	Thr 240
Ile	Arg	Val	Thr	Val	Cys	Glu	Gly	Lys	Asn	Leu	Leu	Gln	Arg	Ala	Asn

245 250 255

Glu Leu Val Asn Pro Asp Val Val Gln Asp Val Asp Ala Ala Thr Ala
260 265 270

Thr Arg Gly Arg Ser Ala Ala Ser Arg Pro Thr Glu Arg Pro Arg Ala 275 280 285

Pro Ala Arg Ser Ala Ser Arg Pro Arg Pro Val Glu Glu Phe 290 295 300

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<211> 120

<212> DNA

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<220>

<221> CDS

<222> (4)..(120)

<400> 41

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Met Asp Val Asp Ala Ala Thr Ala Thr Arg Gly Arg Ser Ala Ala

1 5 10 15

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<213> Artificial Sequence

<400> 42

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Arg Pro Thr Glu Arg Pro Arg Ala Pro Ala Arg Ser Ala Ser Arg Pro
20 25 30

Arg Arg Pro Val Glu Glu Phe

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aggaggtgga tctgc
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<400> 44
Glu Arg Met Arg Arg Pro
  1
                  5
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<223> Description of Artificial Sequence: consensus
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Glu Arg Met Pro Pro Arg Arg Asp
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